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| 09/891,023 | 06/25/2001 | Damir Janigro | 26336-8 | 9460 |

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Raymond A. Miller
c/o Pepper Hamilton LLP
500 Grant Street
50th Floor
Pittsburgh, PA 15219-2502

| EXAMINER | |
|---|---|
| NICHOLS, CHRISTOPHER J | |
| ART UNIT | PAPER NUMBER |
| 1647 | 12 |

DATE MAILED: 08/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/891,023 | JANIGRO ET AL. | |
| | Examiner | Art Unit | |
| | Christopher Nichols, Ph.D. | 1647 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *18 June 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-7 and 22-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,22-36,39 and 40* is/are rejected.

7)☒ Claim(s) *37,38 and 41-43* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☒ The proposed drawing correction filed on *18 June 2003* is: a)☐ approved b)☒ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4 .
4) ☒ Interview Summary (PTO-413) Paper No(s). 9 .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

## DETAILED ACTION

### *Status of Application, Amendments, and/or Claims*

1. The Amendment filed 18 June 2003 (Paper No. 11) has been received and entered in full. Claims 8-21 have been cancelled and claims 22-43 have been added. Claims 1 and 7 have been amended.

### *Withdrawn Objections And/Or Rejections*

2. The objection to the drawings as set forth at pp. 3 ¶4 in the previous Office Action (Paper No. 8, 7 February 2003) is *withdrawn* in view of Applicant's amendments (Paper No. 11, 18 June 2003).

3. The objection to the Specification as set forth at pp. 3 ¶5 in the previous Office Action (Paper No. 8, 7 February 2003) is *withdrawn* in view of Applicant's amendments (Paper No. 11, 18 June 2003).

### *Maintained Objections And/Or Rejections*

4. The rejection of claims 1-6 under 35 U.S.C. §102(b) as anticipated by Westaby *et al.* (1996) "Serum S100 Protein: A Potential Marker for Cerebral Events During Cardiopulmonary Bypass." Ann Thorac Surg **61**: 88-92 is *maintained* for the reasons as set forth at pp. 4 ¶6 in the previous Office Action (Paper No. 8, 7 February 2003).

5. The Applicant traverses said rejection on the following grounds: (a) Temporal Issues: the blood samples are derived from subjects prior to the manifestation of neuronal damage in said subject, (b) Type of Subject Aspects: subjects are free of neuronal damage or free of symptoms

of brain damage at the time of the diagnosis, (c) Varying Levels of S100β: Correlated S100β with permeability of the blood brain barrier (BBB) without neuronal damage and permeability of the BBB with neuronal damage. Applicant's arguments have been fully considered but are not deemed to be persuasive for the following reasons.

6. On "(a)", Westaby *et al.* teaches the method in "Thirty-four patients without neurological problems" (pp. 88). Therefore the newly added limitation fails to exclude the method as taught by Westaby *et al.*

7. On "(b)", Westaby *et al.* teaches the method in "Thirty-four patients without neurological problems" (pp. 88). This includes patients who are "subjects are free of neuronal damage or free of symptoms of brain damage at the time of the diagnosis".

8. On "(c)", Westaby *et al.* states:

"The highly significant correlation between serum S100 level and duration of cardiopulmonary bypass in this set of patients without neurologic signs or symptoms suggests that subclinical cerebral injury or increased permeability of the blood-brain barrier occurs progressively in a dose-related fashion." (pp. 90)

Therefore Westaby *et al.* meets the limitations as set forth by the Applicant in both neuronal damage and instances without neuronal damage in which S100β serum levels are elevated.

9. Thus the rejection of claims 1-6 under 35 U.S.C. §102(b) is maintained.

10. The rejection of claims **1-7** under 35 U.S.C. §103(a) as being upatentable over Westaby *et al.* (1996) "Serum S100 Protein: A Potential Marker for Cerebral Events During Cardiopulmonary Bypass." Ann. Thorac. Surg. **61**: 88-92 [**IDS #BG**] and Herrmann *et al.* (2000) "Release of Glial Tissue-Specific Proteins After Acute Stroke." Stroke **31**: 2670-2677 in view of Strachan *et al.* (1999) "Evaluation of Serum Markers of Neuronal Damage Following Severe

Hypoglycemia in Adults with Insulin-treated Diabetes Mellitus." Diabetes/Metabolism Research and Reviews **15**: 9-12 [**IDS #BB**] is *maintained* for the reasons as set forth at pp. 5-7 ¶7-14 in the previous Office Action (Paper No. 8, 7 February 2003). This rejection now includes newly added claims 22-26.

11. The Applicant traverses said rejection on the following grounds: (a) Temporal Issues: the blood samples are derived from subjects prior to the manifestation of neuronal damage in said subject, (b) Type of Subject Aspects: subjects are free of neuronal damage or free of symptoms of brain damage at the time of the diagnosis, (c) Varying Levels of S100β: Correlated S100β with permeability of the blood brain barrier (BBB) without neuronal damage and permeability of the BBB with neuronal damage. Applicant's arguments have been fully considered but are not deemed to be persuasive for the following reasons.

12. On "(a)", Westaby *et al.* teaches the method in "Thirty-four patients without neurological problems" (pp. 88). Therefore the newly added limitation fails to exclude the method as taught by Westaby *et al.*

13. On "(b)", Westaby *et al.* teaches the method in "Thirty-four patients without neurological problems" (pp. 88). This includes patients who are "subjects are free of neuronal damage or free of symptoms of brain damage at the time of the diagnosis".

14. On "(c)", Westaby *et al.* states:

> "The highly significant correlation between serum S100 level and duration of cardiopulmonary bypass in this set of patients without neurologic signs or symptoms suggests that subclinical cerebral injury or increased permeability of the blood-brain barrier occurs progressively in a dose-related fashion." (pp. 90)

15. Therefore Westaby *et al.* meets the limitations as set forth by the Applicant in both neuronal damage and instances without neuronal damage in which S100β serum levels are elevated.

16. On claim 22, this claim contains limitations that were in claim 7 as originally presented. Claims 23 and 24 are meet by Herrmann *et al.* (2000) who teaches a correlation between CT scans and serum S-100β and GFAP levels in patients (Figure 4). Claim 25 is meet by Westaby *et al.* who teaches that the S100 levels of blood samples are taken prior to surgery thus a "previous point in time". Claim 26 is inherent in the method as taught by Westaby *et al.* which teaches the comparison of S100 serum levels before and after surgery (Table 1). The newly added claims 22-26, do not add limitations which are not meet by the references used in the previous Office Action (Paper No. 8, 7 February 2003).

17. Thus the rejection of claims 1-7 and newly added claims 22-26 under 35 U.S.C. §103(a) is maintained.

## *New Objections And/Or Rejections*

### *Drawings*

18. The drawings are objected to because Figure 3 has two components and should be labeled "A" and "B". A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

### *Claim Objections*

19. Claims 37, 38, 41, 42, and 43 are objected to because of the following informalities: said claims depend from rejected claims. Appropriate correction is required.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

20. Claims **5, 6, 7, 25, 26, 29, 30, 32, 34,** and **36** are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

21. The term "stages of diseased states" in claims 5, 29, and 34 is a relative term which renders the claim indefinite. The term " stages of diseased states " is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is not clear from the Specification or the prior art as to what the metes and bounds of these terms are.

22. The term "neuronal distress" in claims 6, 7, 30, and 39 is a relative term which renders the claim indefinite. The term "neuronal distress" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is not clear from the Specification or the prior art as to what the metes and bounds of these terms are.

23. The term "previous point in time" in claim 25 is a relative term which renders the claim indefinite. The term "previous point in time" is not defined by the claim, the specification does

not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is not clear from the Specification or the prior art as to what the metes and bounds of these terms are.

24. The term "normal levels" in claim 26 is a relative term which renders the claim indefinite. The term "normal levels" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is not clear from the Specification or the prior art as to what the metes and bounds of these terms are.

25. The term "statistically relevant" in claims 32 and 36 is a relative term which renders the claim indefinite. The term "normal levels" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is not clear from the Specification or the prior art as to what the metes and bounds of these terms are.

26. Claims **2, 28, and 35** are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: how samples are "scored".

27. Claims **7, 30, and 39** are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: how markers of neuronal distress are "monitored".

### *Claim Rejections - 35 USC § 102*

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

28. Claims **1, 6, 25, 26, 27, 28, 32, 33,** and **36** are rejected under 35 U.S.C. 102(b) as being anticipated by Wong *et al.* (1999) "S-100β Release in Hypothermic Circulatory Arrest and Coronary Artery Surgery." Ann Thorac Surg **67**: 1911-1914 [**IDS#BF**]. Wong *et al.* teaches the measurement of S100β (synonymous with S-100β) serum levels in patients without neuronal damage before and after surgery independent of indicators of neuronal distress as an indicator of blood brain barrier permeability thus meeting the limitations of claims 1, 27, 33, and 36 (Figure 2; pp. 1913). Wong *et al.*'s S100b measurements were made independent of indicators of neuronal distress and were compared between two time points, the control being pre-operative and the second being post-operative thus meeting the limitations of claims 6, 25, 27 (Figures 2 &3; pp. 1913-1914). Wong *et al.* teaches that elevated S100β levels are indicative of increased permeability of the blood-brain barrier thus meeting the limitations of claim 28 (pp. 1913). Wong *et al.* teaches that the measurement of S100β levels over the course of time including pre-operative, and two post-operative time points to assess permeability of the BBB thus meeting the limitations of claim 32 (pp. 1913; Figure 3).

29. Claims **33-35** are rejected under 35 U.S.C. 102(b) as being anticipated by Erb *et al.* (May 2000) "S-100 After Correction of Congenital Heart Defects in Neonates: Is it a Reliable Marker for Cerebral Damage?" Ann Thorac Surg **69**(5): 1515-1519. Erb *et al.* teaches the measurement of S100 levels in five study populations including "Healthy" which is taken by the Examiner to

mean "free of symptoms of brain damage at the time of diagnosis" and since the "Healthy" population are still neonates and Erb *et al.* teaches that neonates are susceptible to brain damage due to their underdeveloped nervous systems it meets the limitations of claim 33 (Table 1; pp. 1518). Erb *et al.* also teaches a method of successive measurements of serum S100 levels to track the recovery or decline of neonate patients thus meeting the limitations of claim 34 (Figures 1-3). Erb *et al.* also teaches that elevated S100 levels are indicative of increased BBB permeability in this instant case due to an underdeveloped BBB thus meeting the limitations of claim 35 (pp. 1518).

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

30. Claims **27, 28, 29, 30, 31, 32, 36, 39, and 40** are rejected under 35 U.S.C. 103(a) as being unpatentable over Westaby *et al.* (1996) "Serum S100 Protein: A Potential Marker for Cerebral Events During Cardiopulmonary Bypass." Ann Thorac Surg **61**: 88-92 **[IDS #BG]** and

Herrmann *et al.* (2000) "Release of Glial Tissue-Specific Proteins After Acute Stroke." Stroke **31**: 2670-2677 in view of Strachan *et al.* (1999) "Evaluation of Serum Markers of Neuronal Damage Following Severe Hypoglycemia in Adults with Insulin-treated Diabetes Mellitus." Diabetes/Metabolism Research and Reviews **15**: 9-12 [**IDS #BB**].

31. Westaby *et al.* (1996) discloses a method of measuring S100β in human blood samples via form of immunoprecipitation (pp. 89 "*The Assay*"). Westaby *et al.* (1996) teaches that elevated S100β levels in blood is indicative of increased blood brain barrier (BBB) permeability in 34 patients without neurologic problems thus meeting the limitations of claims 27, 28, and 36 (pp. 88, pp. 91, Figure 1). Westaby *et al.* also teaches the measurement of S100β serum levels are three time points, before, during, and after surgery thus meeting the limitations of claim 32 (Table 1). Westaby *et al.* does not teach, however, that levels of S100β protein in blood samples over time are indicative of the stages of diseased states or the use of a combination of measuring NSE and/or GFAP with S100β serum levels.

32. Herrmann *et al.* (2000) teaches the use of an immunoassay to measure GFAP serum levels as an indicator of neuronal distress (pp. 2671-2672 "***Neurobiochemical Analysis***", Figures 1-4). Herrmann *et al.* (2000) also suggests the use of immunoassay measurement of S100β and GFAP as useful over the course of recovering from injury to determine brain lesion size, neurological status, and the outcome of recovery of patients thus meeting the limitations of claims 29, 30, 31, 39, and 40 (pp. 2674-2676 "**Discussion**"). Herrmann *et al.* (2000) mentions but does not teach, however, the use of detecting neuronal-specific enolase (NSE) as a measure of neuronal distress/injury.

33. Strachan *et al.* (1999) teaches a method of determining NSE and S100β levels in serum using an immunoprecipitation assay (pp. 7 "**Measurements of serum NSE and S-100 concentrations**", Figures 3-5). Strachan *et al.* (1999) teaches the determination of NSE and S100β levels in serum as part of an analysis of the stages of Type 1 diabetes and evaluation of treatment regiments thus meeting the limitations of claims 29, 30, 31, 39, and 40 (pp. 7 "**Statistical analyses**", pp. 7-8 "**Case histories**").

34. Thus, it would have been obvious to a person of ordinary skill in the art at the time of the invention to combine an immunoassay measurement of serum S100β levels as taught by Westaby *et al.* (1996) with an immunoassay measurement of serum GFAP as taught by Herrmann *et al.* (2000) and/or NSE levels as taught by Strachan *et al.* (1999) as a method of diagnosing blood brain barrier permeability based on the S100β levels and signs of neuronal distress as determined by the serum NSE and/or GFAP levels [Westaby *et al.* (1996) pp. 90-91; Herrmann *et al.* (2000) pp. 2670 "***Conclusions***", pp. 2674-2676 "**Discussion**"; Strachan et al. (1999) pp. 5 "**Conclusions**", pp. 6, pp. 10-11 "**Discussion**"].

35. A person of ordinary skill in the art at the time of the invention would have been motivated to make these modifications because the standard method of measuring S100β involved a spinal tap, a painful and difficult procedure. In addition, by measuring serum levels of the respective proteins, multiple measurements could be made more efficiently and with less discomfort to the patient over the course of a disease and/or corresponding therapy [Westaby et al. (1996) pp. 90-91; Herrmann *et al.* (2000) pp. 2670 "***Conclusions***", pp. 2674-2676 "**Discussion**"; Strachan et al. (1999) pp. 5 "**Conclusions**", pp. 6, pp. 10-11 "**Discussion**"].

36. A person of ordinary skill in the art at the time of the invention would have a reasonable expectation of success in making the above mentioned modifications because GFAP, and NSE were known to be associated with neuronal distress/injury and S100β was known to be associated with blood brain barrier permeability. Furthermore, S100β, GFAP, and NSE were all successfully measured in human blood samples via an immunoassay at the time of the invention [Westaby *et al.* (1996) pp. 90-91; Herrmann et al. (2000) pp. 2670 "***Conclusions***", pp. 2674-2676 "**Discussion**"; Strachan et al. (1999) pp. 5 "**Conclusions**", pp. 6, pp. 10-11 "**Discussion**"].

37. Thus the invention as a whole was *prima facia* obvious over the prior art.

***Summary***

38. Claims 1-7, 22-36, 39, and 40 are hereby rejected.

39. The following articles, patents, and published patent applications were found by the Examiner during the prior art search and are here made of note:

a. Biberthaler *et al.* (2000) "Influence of Alcohol Exposure on S-100b Serum Levels." Acta Neurochir [Suppl] **76**: 177-179

40. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

41. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

## *Conclusion*

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Christopher James Nichols, Ph.D.** whose telephone number is 703-305-3955. The examiner can normally be reached on Monday through Friday, 8:00AM to 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Gary Kunz, Ph.D.** can be reached on 703-308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications. The fax phone numbers for the customer service center is 703-872-9305

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Elizabeth C Kemmerer

CJN
August 19, 2003

ELIZABETH KEMMERER
PRIMARY EXAMINER

# REVISED AMENDMENT PRACTICE: 37 CFR 1.121 CHANGED COMPLIANCE IS MANDATORY - Effective Date: July 30, 2003

All amendments filed on or after the effective date noted above must comply with revised 37 CFR 1.121. See Final Rule: **Changes To Implement Electronic Maintenance of Official Patent Application Records** (68 *Fed. Reg.* 38611 (June 30, 2003), posted on the Office's website at: http://www.uspto.gov/web/patents/ifw/ with related information. The amendment practice set forth in revised 37 CFR 1.121, and described below, replaces the voluntary revised amendment format available to applicants since February 2003. **NOTE: STRICT COMPLIANCE WITH THE REVISED 37 CFR 1.121 IS REQUIRED AS OF THE EFFECTIVE DATE (July 30, 2003).** The Office will notify applicants of amendments that are not accepted because they do not comply with revised 37 CFR 1.121 via a Notice of Non-Compliant Amendment. See MPEP 714.03 (Rev. 1, Feb. 2003). The non-compliant section(s) will have to be corrected and the entire corrected section(s) resubmitted within a set period.

***Bold underlined italic font has been used below to highlight the major differences between the revised 37 CFR 1.121 and the voluntary revised amendment format that applicants could use since February, 2003.***

Note: The amendment practice for **reissues** and **reexamination proceedings**, except for drawings, has not changed.

## REVISED AMENDMENT PRACTICE

**I. Begin each section of an amendment document on a separate sheet:**

Each section of an amendment document (*e.g.*, Specification Amendments, Claim Amendments, Drawing Amendments, and Remarks) must begin on a separate sheet. Starting each separate section on a new page will facilitate the process of separately indexing and scanning each section of an amendment document for placement in an image file wrapper.

**II. Two versions of amended part(s) no longer required:**

**37 CFR 1.121 has been revised to no longer require two versions (a clean version and a marked up version) of each replacement paragraph or section, or amended claim. Note, however, the requirements for a clean version and a marked up version for substitute specifications under 37 CFR 1.125 have been retained.**

**A) Amendments to the claims:**

Each amendment document that includes a change to an existing claim, cancellation of a claim or submission of a new claim, **must include a complete listing** of all claims in the application. After each claim number in the listing, the status must be indicated in a parenthetical expression, and **the text of each pending claim** (with markings to show current changes) must be presented. The claims in the listing will replace all prior claims in the application.

(1) The current status of all of the claims in the application, including any previously canceled, not entered or withdrawn claims, must be given in a parenthetical expression following the claim number using only one of the following seven status identifiers: (original), (currently amended), (canceled), (withdrawn), (new), *(previously presented) and (not entered).* The text of all pending claims, *including withdrawn claims,* must be submitted each time any claim is amended. Canceled *and not entered* claims must be indicated by only the claim number and status, without presenting the text of the claims.

(2) The text of all claims being currently amended must be presented in the claim listing with markings to indicate the changes that have been made relative to the immediate prior version. The changes in any amended claim must be shown by underlining (for added matter) or strikethrough (for deleted matter) with 2 exceptions: (1) for *deletion of five characters or fewer, double brackets may be used (e.g., [[eroor]]); and (2) if strikethrough cannot be easily perceived (e.g., deletion of the number "4" or certain punctuation marks), double brackets must be used (e.g., [[4]]). As an alternative to using double brackets, however, extra portions of text may be included before and after text being deleted, all in strikethrough, followed by including and underlining the extra text with the desired change* (*e.g.*, ~~*number 4 as*~~ *number 14 as*). An accompanying clean version is not required and should not be presented. Only claims of the status "currently amended," and "withdrawn" that are being amended, may include markings.

(3) The text of pending claims not being currently amended, *including withdrawn claims,* must be presented in the claim listing in clean version, *i.e.*, without any markings. Any claim text presented in clean version will constitute an assertion that it has not been changed relative to the immediate prior version except to omit markings that may have been present in the immediate prior version of the claims.

(4) A claim being canceled must be listed in the claim listing with the status identifier "canceled"; the text of the claim must not be presented. Providing an instruction to cancel is optional.
(5) Any claims added by amendment must be presented in the claim listing with the status identifier "(new)"; the text of the claim must not be underlined.
(6) All of the claims in the claim listing must be presented in ascending numerical order. Consecutive canceled, or not entered, claims may be aggregated into one statement (*e.g.*, Claims 1 - 5 (canceled)).

**Example of listing of claims (use of the word "claim" before the claim number is optional):**

Claims 1-5 (canceled)

Claim 6 (previously presented): A bucket with a handle.

Claim 7 (withdrawn): A handle comprising an elongated wire.

Claim 8 (withdrawn): The handle of claim 7 further comprising a plastic grip.

Claim 9 (currently amended): A bucket with a ~~green~~ blue handle.

Claim 10 (original): The bucket of claim 9 wherein the handle is made of wood.

Claim 11 (canceled)

Claim 12 (not entered)

Claim 13 (new): A bucket with plastic sides and bottom.

**B) Amendments to the specification:**
Amendments to the specification, including the abstract, must be made by presenting a replacement paragraph or section or abstract marked up to show changes made relative to the immediate prior version. An accompanying clean version is not required and should not be presented. Newly added paragraphs or sections, including a new abstract (instead of a replacement abstract), must not be underlined. A replacement or new abstract must be submitted on a separate sheet, 37 CFR 1.72. If a substitute specification is being submitted to incorporate extensive amendments, both a clean version (which will be entered) and a marked up version must be submitted as per 37 CFR 1.125.

The changes in any replacement paragraph or section, or substitute specification must be shown by underlining (for added matter) or strikethrough (for deleted matter) with 2 exceptions: (1) for *deletion of five characters or fewer, double brackets may be used (e.g., [[eroor]]); and (2) if strikethrough cannot be easily perceived (e.g., deletion of the number "4" or certain punctuation marks), double brackets must be used (e.g., [[4]]). As an alternative to using double brackets, however, extra portions of text may be included before and after text being deleted, all in strikethrough, followed by including and underlining the extra text with the desired change* (*e.g.*, ~~*number 4 as*~~ *number 14 as)*

C) **Amendments to drawing figures:**
Drawing changes must be made by presenting replacement figures which incorporate the desired changes and which comply with 37 CFR 1.84. An explanation of the changes made must be presented either in the drawing amendments, or remarks, section of the amendment, *and may be accompanied by a marked-up copy of one or more of the figures being amended, with annotations.* Any replacement drawing sheet must *be identified in the top margin as "Replacement Sheet"* and include all of the figures appearing on the immediate prior version of the sheet, even though only one figure may be amended. *Any marked-up (annotated) copy showing changes must be labeled "Annotated Marked-up Drawings" and accompany the replacement sheet in the amendment (e.g., as an appendix).* The figure or figure number of the amended drawing(s) must **not** be labeled as "amended." If the changes to the drawing figure(s) are not accepted by the examiner, applicant will be notified of any required corrective action in the next Office action. No further drawing submission will be required, unless applicant is notified.

Questions regarding the submission of amendments pursuant to the revised practice set forth in this flyer should be directed to: Elizabeth Dougherty or Gena Jones, Legal Advisors, or Joe Narcavage, Senior Special Projects Examiner, Office of Patent Legal Administration, by e-mail to patentpractice@uspto.gov or by phone at (703) 305-1616.